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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/047,072	01/15/2002	Ralph M. Steinman	MER-011CN/112917-144	7452

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EXAMINER	
EWOLDT, GERALD R	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 03/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/047,072	STEINMAN ET AL.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-6 and 10-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-6 and 10-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

HL

DETAILED ACTION

1. Claims 1-6 and 10-12 are being acted upon.

2. Applicant's amendment and remarks, filed 1/28/05, are acknowledged. In view of Applicant's amendment, all previous rejections under 35 U.S.C. 112, first paragraph, for the introduction of new matter into the claims, have been withdrawn. Upon reconsideration, the previous rejection under the second paragraph of 35 U.S.C. 112 has also been withdrawn.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-6 and 10-12 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

As set forth previously, there is insufficient written description to show that Applicant was in possession of a factor in which to culture pluripotential cells which would cause them to express characteristics of DCs, for the reasons of record as set forth in the papers mailed 4/02/03, 1/16/04, and 7/28/04.

Applicant's arguments, filed 1/28/05, have been fully considered but they are not persuasive. Applicant argues that, "Page 27 of the specification describes assays which can be used to identify the factor. Applicants respectfully aver that one of ordinary skill in the art, at the time the invention was filed, would have been able to identify the factor following the guidance provided by the Application".

Assuming *arguendo* that the factor of the instant claims exists, it remains the Examiner's position that the specification fails to adequately describe said factor. Absent the actual identification of said factor, an adequate written

description would include a description including both a common structure and a common function of said factor. In the instant case, Applicant has described a function, i.e., the ability to generate mature stable DCs from immature DCs, but no common structure. Applicant has disclosed sources of said factor, e.g., monocyte conditioned medium, but a source is not a structure. Thus, it remains the Examiner's position that the disclosure of a function and an assay by which the unknown factor can be identified comprises an inadequate written description of the factor of the instant claims.

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

6. Claims 1-6 and 10-12 stand rejected under 35 U.S.C. 102(e) as being clearly anticipated by U.S. Patent No. 5,994,126 (of record) as evidenced by Kiertscher et al. (1996).

As set forth previously, the '126 patent teaches an *in vitro* method of producing DCs comprising culturing pluripotential cells comprising monocytes (which are inherently $CD14^+$) or mononuclear cells (both components of PBMCs) in about 200U/ml to about 2000U/ml of a "factor" comprising GM-CSF and additionally IL-4 (see particularly column 16, lines 43-45 and Example 1). Note that Claims 11 and 12 merely recite well known properties inherent to DCs, i.e., high level expression of MHC molecules and the capacity to stimulate resting T cells. Kiertscher et al. demonstrates that PBMC cultured in GM-CSF and IL-4 (Figure 1), the method of the '126 patent, results in the

DCs of the instant claims, e.g., DCs with increased CD83 expression (Table I).

Applicant's arguments, filed 1/28/05, have been fully considered but they are not persuasive. Applicant argues that, Claim 1 as now written comprises a two step culture mechanism not disclosed in the prior art.

Applicant is advised that claims recite no limitation that step b) must follow step a) in any particular time frame. Thus, the continuous culture of the '126 reference meets the limitations of the claims. In particular, step b) requires only that immature DCs be cultured for sufficient time in PBMC conditioned medium for mature stable DCs, as demonstrated by the induction of certain characteristics, e.g., CD83 expression, to be generated. Note that the specification discloses that the conditioned medium of the claims comprises any medium in which PBMC have been cultured (pages 18 and 19); thus, the medium of the reference would be considered to be the conditioned medium of the instant specification and accordingly, comprise the factor of the instant claims. Given the culture of Example 1 in the reference lasts 3 weeks, the method of the reference would inherently comprise the claimed method and inherently produce mature stable DCs.

7. Claims 1-6 and 10-12 stand rejected under 35 U.S.C. 102(b) as being clearly anticipated by Romani et al. (1994, of record) as evidenced by Caux et al. (of record).

As set forth previously, Romani et al. teaches an *in vitro* method of producing DCs comprising culturing pluripotential cells comprising monocytes (which are inherently $CD14^+$) or mononuclear cells (both components of PBMCs) in about 200U/ml to about 2000U/ml of a "factor" comprising GM-CSF and additionally TNF-α (see particularly page 84, **Materials and Methods**). Note that Claims 11 and 12 merely recite well known properties inherent to DCs, i.e., high level expression of MHC molecules and the capacity to stimulate resting T cells. Caux et al. (1996) demonstrates that pluripotential cells cultured in GM-CSF and TNF-α (Materials and Methods), the method of Romani et al., results in the DCs of the instant claims, e.g., DCs with increased CD83 and CD86 expression (Figure 5).

Applicant's arguments, filed 1/28/05, have been fully considered but they are not persuasive. Applicant argues that,

Claim 1 as now written comprises a two step culture mechanism not disclosed in the prior art. Applicant further argues that the DCs of the reference are immature DCs.

Regarding the now recited two step culture method, see Section 6 above. Regarding the assertion that the DCs of the reference are immature, the reference does not indicate such. The reference teaches a culture that would include pluripotential cells in PBMC conditioned medium for 5 to 7 days. The instant specification discloses that immature DCs are generated in about 6 to 10 days and mature DCs are obtained by further culture in conditioned medium "within approximately 3 days" (pages 18-19). Thus, the culture of the reference falls within the time frame disclosed in the instant specification, and the method of the reference would inherently comprise the claimed method and inherently produce mature stable DCs.

8. The following are new grounds of rejection necessitated by Applicant's amendment.

9. Claims 1-6 and 10-12 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically, a method wherein the maturation factor is present in "macrophage conditioned medium" as recited in Claim 1.

Applicant indicates that support for the new amendment can be found at pages 5, 6, and 18 of the specification but support for the limitation as set forth above has not been found.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 1-6 and 10-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to

particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically: "A method for producing dendritic cells" resulting in "stable mature dendritic cells" is vague and indefinite as the result of the method does not match the preamble of the method. Note that the generic "dendritic cells" of the preamble comprises a much larger genus than the "stable mature dendritic cells" that result from performing the claimed method. Applicant is advised that the recitation of a method for producing stable mature dendritic cells resulting in stable mature dendritic cells would obviate the rejection.

12. Applicant's amendment or action necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

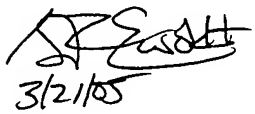
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

15. **Please Note**: Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR

or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). Inquiries of a general nature may also be directed to the Technology Center 1600 Receptionist at (571) 272-1600.



3/21/05

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